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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/663,533 | 09/16/2003 | Adam M. Gilbert | AM100279/WYNC-0677 | 3576 |
| 23377 | 7590 | 09/21/2004 | EXAMINER | |
| WOODCOCK WASHBURN LLP ONE LIBERTY PLACE, 46TH FLOOR 1650 MARKET STREET PHILADELPHIA, PA 19103 | | | HUANG, EVELYN MEI | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1625 | |

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/663,533

Applicant(s)

GILBERT ET AL.

Examiner

Evelyn Huang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26 and 33-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26, 33-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

1. Claims 26, 33-52 are pending. Claims 1-25, 27-32 have been canceled according to the preliminary amendment filed on 9-16-2-2003.

Claim Rejections - 35 USC § 112

2. The rejection for Claims 26, 33-52 under 35 U.S.C. 112, second paragraph, is withdrawn upon reconsideration in view of Applicant's remarks.

Claim Rejections - 35 USC § 112(1)

3. The rejection for Claims 26, 33-52 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained for reasons of record.

Applicant maintains that the procedures for the 5-HT transporter binding assays, 5-HT_{1A} receptor binding assays, and the assay for the assessment of the antagonist activity, are provided on pages 9-10 of the specification. Results have been shown for Examples 1-11 on page 11 of the specification. As such, the inventive compound would be useful for treatment of neurodegenerative diseases, eating disorders, disorders of thermoregulation, sleep dysfunction, or sexual dysfunction as there is nexus between the antagonism of 5HT_{1A} and the treatment of these disorders.

On the contrary, while 5HT_{1A} receptor has been implicated in many physiological responses, and 5HT_{1A} receptor agonist has been shown to have anxiological and antidepressant activity, the nexus between neurodegenerative diseases, eating disorders, disorders of thermoregulation, sleep dysfunction, or sexual dysfunction as recited and 5HT_{1A} receptor has not been fully established. For example, while 5HT_{1A} receptor agonist evokes hypothermia, inhibition of 5HT synthesis and 5-HT lesions do not prevent hypothermia when the agonists are injected in rats (Barnes, page 1092). Some of the responses elicited by a 5HT_{1A} receptor agonist, 8-OH-PAT, such as hyperphagia (Fletcher et al. Psychopharmacology, 1990, 100(2): 188-94, abstract), altered sexual behavior (Matuszewich et al. Brain Research 1999, 820(1-2): 55-62,

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abstract), are not reversed by a 5HT_{1A} receptor antagonist, thereby suggesting that these effects are not mediated by the 5HT_{1A} receptor.

Furthermore, there is no umbrella drug known to be effective in treating all types of 'eating disorders' (which encompass the opposing hyperphagia and anorexia), 'sexual dysfunction' (which embrace the conflicting conditions involving both the inhibitory and stimulatory sexual behaviors), 'disorders of thermoregulation' (which includes the opposing hypothermia and hyperthermia), 'sleep dysfunction' (which covers both insomnia and narcolepsy) and neurodegenerative diseases of any kind. Since they are general classes of disorders embracing opposing and conflicting conditions arising from diverse origins, one of ordinary skill in the art recognizes that it is impossible to use a single 5HT_{1A} receptor antagonist compound of the instant to treat all these contradictory disorders.

Applicant contends that a lack of in vivo working examples with respect to methods of treating neurodegenerative diseases, eating disorders, disorders of thermoregulation, sleep dysfunction, sexual dysfunction does not automatically make the patent non-enabling. 35 U.S.C. 112 first paragraph does not demand a 'working example'.

The rejection, however, is not based solely on the lack of in vivo working examples. The examiner agrees that a working example is not required to satisfy the enablement requirement, and some experimentation is permitted and every claimed embodiment need not be shown to possess the asserted activity. However, there should be a showing commensurate in scope with the claims. In the instant 5HT_{1A} antagonist art, where there is a high degree of unpredictability exists, in that slight change in the structure of the compound would drastically alter its affinity and selectivity (Wijngaarden, Recl. Trav. Chim. Pays-Bas, 1993, 112:126-130, pages 129-130, Fig. 6, Fig. 7, Fig. 8, and the in vitro binding data do not necessarily reflect the in vivo activity, the required disclosure will be greater than for the disclosure of an invention involving a predictable factor such as a mechanical or electrical element. In re Vaeck, 20 USPQ 2d 1438.

In conclusion, in view of the state of the art, the high degree of unpredictability of the art, the limited working examples, the scope of the claims does not commensurate with that of the objective enablement. Insufficient teaching and guidance have not been provided in the

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specification to enable one of ordinary skill in the art to make and use the invention as claimed without undue experimentation.

Double Patenting

4. The timely filed terminal disclaimer has obviated the obviousness-type double patenting rejection over claims 22-28 of U.S. Patent No. 6656951.

Conclusion

5. No claims are allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Evelyn Huang

Primary Examiner

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